DEPARTMENT OF HEALTH AND HUMAN SERVICES

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Food and Drug Administration
Florida District
555 Winderley Place
Suite 200
Maitland, Florida 32751
Telephone: 407-475-4731

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

WARNING LETTER

FLA-05-07

November 9, 2004

Mr. Steven M. Dietz
President
South Florida Medical Corporation
6462 E Rogers Circle
Boca Raton, FL 33487

Dear Mr. Dietz:

The Food and Drug Administration (FDA) inspected your medical oxygen gas transfilling facility located at the above address on August 18 to August 20, 2004. Medical gases are drug products as defined in section 201(g) of the Federal Food, Drug, and Cosmetic Act (the Act). Our inspection found significant deviations from the Current Good Manufacturing Practice (CGMP) regulations for drug products, set forth in Title 21, Code of Federal Regulations, (21 CFR), Parts 210 and 211. These deviations cause your product, Oxygen USP, to be adulterated within the meaning of section 501(a) (2) (B) of the Act, in that the methods used in or the facilities or controls used for the manufacturing, processing, packing, storage or holding of your product are not in conformance with CGMP regulations.

The deviations observed during the inspection include the following:

1. Failure to perform testing to determine satisfactory conformance to final specifications for the finished drug product, including identity and strength of the active ingredient [21 CFR 211.165(a)].

   For example, finished product testing is not performed on filled cylinders of Oxygen USP, prior to their release for distribution.

2. Failure to establish and follow adequate written procedures for production and process control designed to assure that drug products have the identity, strength, quality and purity they purport or are represented to possess [21 CFR 211.100(a) and (b)].

   For example, neither the general "model" written procedures, titled "Food and Drug Administration Program Guidelines and Compliance," provided to your firm by the supplier of the transfilling equipment or the instructions specific to transfilling operations used by your firm's filling personnel have been reviewed and approved by a quality control unit. In addition, the "model" procedures are deficient in that they do not require a finished product odor test and

other referenced procedures, such as those for equipment calibration handling of incoming source cylinders, are missing. Procedures requiring checks for hydrostatic retest dates, hammer tests on empty cylinders, and finished product testing, are not followed.

3. Failure to establish scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that drug products conform to appropriate standards of identity, strength, quality, and purity [21 CFR 211.160(b)].

   For example, your firm's written procedures do not address the methods to be used for testing finished drug products. There were no written procedures for operation of the Servomex Oxygen Analyzer. There was no written program for calibration of this instrument as required by 21 CFR 211.160(b)(4) and there were no calibration standards.

4. Failure to establish a quality control unit having the responsibility and authority to approve and reject all components, drug product containers, closures, in –process materials, packaging materials, labeling and drug products and the authority to review production records to assure that no errors have occurred. [21 CFR 211. 22(a)].

   For example, your firm has not established a quality control unit. Personnel with quality control authority have not been designated. There are no written procedures defining its responsibilities or functions.

5. Batch production records for drug products are not reviewed and approved by a quality control unit prior to release of the products [21 CFR 211.192].

   For example, batch production records for Oxygen USP are not reviewed and approved by a person with quality control unit authority.

6. Failure to document each significant step in the manufacture of the drug product [21 CFR 211.188(b)].

   For example, batch records do not document external examinations of cylinders, checks for hydrostatic test dates, prefill odor tests, hammer tests, or valve leak checks.

7. Failure to routinely calibrate automatic or mechanical equipment according to a written program [21 CFR 211.68(a)].

   For example, your firm has not calibrated pressure gauges or thermometers used to monitor the medical oxygen transfilling process.

8. Failure to train employees in the particular operations performed or in current good manufacturing practice regulations as they relate to the employee's functions [21 CFR 211.25(a)].

   For example, employees have received no training in current good manufacturing practice regulations. Both management and staff professed to be unaware of applicable CGMP requirements when interviewed by the FDA Investigator.

9. The drug product does not bear an expiration date determined by appropriate stability testing [21 CFR 211.137(a)].

For example, the expiration date placed by your firm on the labels for Oxygen USP is not based on results from a written program to test the stability of the product in its container- closure system as required by 211.166(a)(4). The expiration date used is copied from the labeling applied to the "H" cylinders used as the source gas for transfilling.

10. Failure to establish and follow written procedures for the cleaning and maintenance of equipment used in the manufacturing, packing and holding of a drug product, describing in sufficient detail the methods, equipment, materials used in cleaning and maintenance operations [21 CFR 211.67(b)(3)].

    For Example, your firm has not established written procedures pertaining to the cleaning and maintenance of equipment used to manufacture Oxygen USP.

11. Failure to examine labeling and packaging materials upon receipt and before use in packaging and labeling of a drug product [21 CFR 211.122(a)].

    For example, your firm had no records to show that Oxygen USP labels are examined upon receipt and before use or compared against an approved master label, to assure correctness.

12. Failure to establish and follow written procedures describing in sufficient detail the control procedures employed for the issuance of labeling [21 CFR 211.125(f)].

    For example, your firm has not established written procedures for labeling issuance.

13. Failure to establish written procedures for describing the handling of all written and oral drug product complaints [21 CFR 211.198(a)].

    For example, your firm does not have a written procedure that addresses handling of complaints.

14. Failure to maintain written records of each drug product complaint received [21 CFR 211.198(b)].

    For example, your firm does not have documentation of complaints received or whether an investigation was conducted.

Your firm must also take prompt action to register with FDA as a drug manufacturer and file a drug listing form for the Oxygen USP. Failure to do so constitutes violations of sections 510(c) and 510(j) of the Act. We acknowledge the steps your firm has already taken toward corrective action in this area. You can find guidance and information regarding regulations for drug products through FDA's internet page for the regulated industry at http://www.fda.gov/oc/industry/.

The above identification of violations is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure adherence with each requirement of the CGMP regulations. Federal agencies are advised of the issuance of all warning letters about drugs so that they may take this information into account when considering the award of contracts. Please note that we will share our inspectional findings with the United States Department of Transportation. You should take prompt action to correct these violations, and you should establish procedures whereby such violations do not recur. Failure to do so may result in regulatory action without further notice. Possible actions include, but are not limited to, seizure and/or injunction.

You should notify this office in writing, within (15) working days of receipt of this letter, of the specific steps you have taken to correct the noted violation(s), including an explanation of each step taken to prevent recurrence of similar violations. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed.

Your reply should be directed to the Food and Drug Administration, Attention: Virginia L. Meeks, Compliance Officer, 555 Winderley Place, Suite 200, Maitland, FL 35271. If you have questions regarding any issue in this letter, please contact Ms. Meeks at (407) 475-4731.

Sincerely,

Elizabeth W. Onmd

for Emma R. Singleton
Director, Florida District